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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/873,106	06/01/2001	Ellis L. Reinherz	1062.1021-004	2390
21005	7590	06/07/2004	EXAMINER	
HAMILTON, BROOK, SMITH & REYNOLDS, P.C. 530 VIRGINIA ROAD P.O. BOX 9133 CONCORD, MA 01742-9133			VANDERVEGT, FRANCOIS P	
			ART UNIT	PAPER NUMBER
			1644	

DATE MAILED: 06/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/873,106	REINHERZ ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	F. Pierre VanderVegt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 03 July 2003.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-61 is/are pending in the application.
- 4a) Of the above claim(s) 1-6,23-43 and 47-53 is/are withdrawn from consideration.
- 5) Claim(s) 11-13,15-17,19-21 and 54 is/are allowed.
- 6) Claim(s) 7-9,14,18,22,44-46 and 55-61 is/are rejected.
- 7) Claim(s) 10 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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#### **DETAILED ACTION**

The Examiner in charge of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to F. Pierre VanderVegt, Ph.D. in Art Unit 1644.

It is noted that in the Final Office Action mailed December 12, 2003 the Examiner did not address newly added claims 54-61, which are drawn to the elected invention. Accordingly, the **Final Office Action mailed December 12, 2003 is hereby vacated** and is replaced by the instant Office Action, which addresses all pending claims that are drawn to the elected invention.

This application claims the benefit of the filing date of provisional application 60/148,815.

New claims 54-61 have been added.

Claims 1-61 are currently pending.

Claims 1-6, 23-43 and 47-53 stand as withdrawn.

Claims 7-22, 44-46 and 54-61 are the subject of examination in the present Office Action.

1. In view of Applicant's amendment and remarks filed July 3, 2003, no outstanding grounds of rejection have been maintained.

2. **The following new grounds of rejection have been necessitated by Applicant's amendment.**

Applicant's arguments with respect to claims 7-9, 12-14, 16-18, 20-22 and 44-46 have been considered but are moot in view of the new ground(s) of rejection.

#### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 7-9, 14, 18, 22, 44-46 and 55-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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Claim 7 and dependent claims 8-9, 14, 18 and 22 are most broadly drawn to an isolated nucleic acid molecule which encodes a protein comprising SEQ ID NO: 2 or a fragment of said protein having the biological activity of the polypeptides of SEQ ID NO: 3 or SEQ ID NO: 9, or the complement of said nucleic acid molecule, a host cell comprising said nucleic acid molecule, and a method of producing said protein comprising said host cell.

The instant disclosure of an isolated nucleic acid molecule which encodes a CD2BP2 protein of SEQ ID NO: 2 derived from human cells does not adequately describe the scope of the claimed genus of nucleic acid molecules which encode a protein comprising a fragment of SEQ ID NO: 2, as recited in claims 7-9, 14, 18 and 22, which encompasses nucleic acid molecules which encode a CD2BP2 from a substantial variety of species or a protein comprising a fragment of SEQ ID NO: 2. The specification does not describe a nucleic acid encoding a CD2BP2 protein from any species other than human nor does the specification describe any other type of protein comprising a fragment of SEQ ID NO: 2, and therefore, the invention encompassing a nucleic acid encoding a CD2BP2 protein derived from all species or other proteins comprising a fragment of SEQ ID NO: 2 having an undisclosed function is not adequately described.

Claim 8 recites “[a]n isolated nucleic acid molecule possessing sequence identity of at least 80% with the nucleic acid molecule of claim 7” wherein said nucleic acid sequence encodes a fragment of SEQ ID NO: 2 has biological activity of SEQ ID NO: 3 or 9, which is a recitation of a genus of polypeptides for which Applicant has disclosed a single species: the polypeptide of SEQ ID NO: 3 or 9. Accordingly, there is no descriptive support for nucleic acid molecules having the activity of SEQ ID NO: 3 or 9 other fragments of SEQ ID NO: 2 comprising SEQ ID NO: 3 or 9.

Furthermore, dependent claim 9 is drawn to “an endogenous gene encoding a protein of SEQ ID NO: 2. The claim reads upon genomic sequences, however genomic sequences have not been described. The only sequence the specification or claims as originally filed describes as encoding SEQ ID NO: 2 is the polynucleotide of SEQ ID NO: 1. SEQ ID NO: 1 is a cDNA sequence and gives no information regarding intervening DNA sequences (introns) that are not translated into the mRNA from which the cDNA of SEQ ID NO: was created. Accordingly, the specification does not provide sufficient written descriptive support for the recitation of “endogenous” genes.

It is noted that a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial

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portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed.

4. Claims 7-9, 14, 18, 22 and 44-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule which encodes the CD2BP2 protein of SEQ ID NO: 2, or a fragment of said protein having CD2BP2 protein activity, wherein said fragment consists of one of the following fragments of a nucleotide encoding CD2BP2: (nucleotides encoding amino acids 129-341 of SEQ ID NO: 2, nucleotides encoding amino acids 225-341 of SEQ ID NO: 2, nucleotides encoding amino acids 256-341 of SEQ ID NO: 2, nucleotides encoding amino acids 256-338 of SEQ ID NO: 2, and nucleotides encoding amino acids 291-317 of SEQ ID NO: 2, (Page 22)), and the complement of said nucleic acid molecule, a host cell comprising said nucleic acid molecule, and a method of producing said protein comprising said host cell, an isolated nucleic acid molecule consisting of a nucleotide sequence consisting of SEQ ID NO: 9, and 10, does not reasonably provide enablement for the broader recitation of an isolated nucleic acid molecule which encodes any protein comprising a fragment of SEQ ID NO: 2 having the activity of SEQ ID NO: 3 or 9, or any nucleic acid molecule encoding a polypeptide possessing 80% identity with a fragment of SEQ ID NO: 2 as recited in claim 8. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 7 and dependent claims 8-9, 14, 18 and 22 are drawn to an isolated nucleic acid molecule which encodes a fragment of SEQ ID NO: 2 protein having an undisclosed biological activity of SEQ ID NO: 3 or 9, or the complement of said nucleic acid molecule, a host cell comprising said nucleic acid molecule, and a method of producing said protein comprising said host cell

The instant specification discloses that human CD2 molecule is found on virtually all T cells and thymocytes and natural killer cells, and the CD2 cytoplasmic tail is important for T cell activation (page 2 of the specification). The mechanism by which the CD2 tail mediates activation is not clear. The specification discloses an intracellular protein termed CD2 binding protein 2 (CD2BP2) of SEQ ID NO: 2 which binds a site containing two PPPGHR (seq ID NO: 10) segments within the cytoplasmic region of CD2 has been described herein and that the CD2 binding region of CD2BP2 includes a 17 amino acid

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binding motif (SEQ ID NO:9) (GP[Y/F] XXXX[M/V]XXWXXXGYF which is also found in yeast and *C. elegans* proteins of unknown function (page 5 of the specification).

The instant disclosure of an isolated nucleic acid molecule which encodes a CD2BP2 protein derived ONLY from human cells does not provide sufficient guidance and direction regarding making any nucleic acid molecule which encodes a CD2BP2 protein derived from any species other than human as encompassed by claims 7-9, 14, 18 and 22. The state of the art does not teach any an isolated nucleic acid molecule which encodes a CD2BP2 protein, and therefore it would require undue experimentation for one of skill in the art to make an isolated nucleic acid molecule which encodes any CD2BP2 protein, other than one derived from human, of SEQ ID NO:1 or encoding SEQ ID NO: 2, without further guidance and direction from the specification.

The instant disclosure of the following fragments of a nucleotide encoding CD2BP2 (SEQ ID NO: 2): (nucleotides encoding amino acids 129-341 of CD2BP2, nucleotides encoding amino acids 225-341 of CD2BP2, nucleotides encoding amino acids 256-341 of CD2BP2, nucleotides encoding amino acids 256-338 of CD2BP2, and nucleotides encoding amino acids 291-317 of CD2BP2, (Page 22)), does not provide sufficient guidance and direction regarding making a nucleic acid molecule which encodes any fragment of CD2BP2 (SEQ ID NO: 2) which has CD2BP2 protein activity, as encompassed by claims 7-9, 14, 18 and 22, (except those disclosed supra), given the disclosed definitions of CD2BP2 activity and of biologically active fragments of CD2BP2 polypeptides, and the state of the art at the time the invention was made.

It would also require undue experimentation for one of skill in the art to make an isolated nucleic acid molecule which encodes a fragment of or a polypeptide with 80% identity to a fragment of SEQ ID NO: 2 that has biological activity of SEQ ID NO: 3 or 9, as encompassed by claims 7-9, 14, 18 and 22, especially given such a broad definition of CD2BP2 activity and given the absence of a disclosure of a single such nucleic acid molecule. Page 28 discloses that nucleic acid molecules encoding derivatives which can be naturally occurring such as in the case of allelic derivatives, or non-naturally occurring resulting from mutagenesis, and include deletion, addition and substitution of one or more nucleotides which can result in conservative or non conservative amino acid changes, including additions and deletions, and also discloses that activities of the encoded polypeptide include, but are not limited to, catalytic activity, binding function, antigenic function and oligomerization function.

However, the structure of an isolated nucleic acid molecule which encodes any active derivative (including proteins with 80% sequence identity) of SEQ ID NO: 2 that has biological activity of SEQ ID NO: 3 or 9 is not conventional in the art and therefore it would require undue experimentation for one of

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skill in the art to make an isolated nucleic acid molecule which encodes any active derivative of CD2BP2 that has CD2BP2 protein activity encompassed by the claimed invention, without further guidance and direction from the specification, especially in view of such a broad definition of CD2BP2 activity and in view of the lack of a compensatory structural or correlative teachings in the prior art of an isolated nucleic acid molecule which encodes a derivative of said protein having said CD2BP2 protein activity.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 44-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims each recite "wherein said nucleotide sequence is heterologous" at the end of the claim. It is unclear exactly what the nucleotide sequence is heterologous to.

#### *Claim Rejections - 35 USC § 102*

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7, 8, 45 and 55-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Percy (submitted to the EMBL data Library on October 1996) as evidenced by NCBI blast search (of record).

Percy teaches a nucleotide sequence derived from *C. elegans* that comprises a nucleotide encoding the amino acid sequence of SEQ ID NO: 9, specifically residues 19-45 of the referenced encoded amino acid sequence. The claims are drawn to an isolated nucleic acid sequence comprising a fragment of SEQ ID NO: 2 that has the biological activity of SEQ ID NO: 9. The claim does not specify what type of biological activity of SEQ ID NO: 9 is intended. Accordingly, the natural biological

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function performed by the protein disclosed by Percy in *C. elegans* satisfies the metes and bounds of the claim. Furthermore, the specification only discloses that:

“it has been discovered that a motif on CD2 (SEQ ID NO: 10) interacts with (e.g., binds) a motif on CD2BP2 (SEQ ID NO: 9, e.g., SEQ ID NO: 3). This discovery provides a method of enhancing or promoting protein-protein interactions between proteins which bear these motifs. That is, a protein which comprises the motif of SEQ ID NO: 10 will interact with a protein which comprises the motif of SEQ ID NO: 9 (e.g., SEQ ID NO: 3) by virtue of the interaction between the two motifs. The proteins can normally (in nature) comprise the specified motifs or can be proteins which do not normally (in nature) comprise the motifs but which have been engineered to contain them.”

Accordingly, the only disclosed biological function of SEQ ID NO: 9 is binding to SEQ ID NO: 10, irrespective of which protein either sequence is a part of. It is respectfully submitted therefore that, even as part of a *C. elegans* protein, the peptide sequence taught by Percy that corresponds to SEQ ID NO: 9 will still bind to the motif defined by SEQ ID NO: 10. The prior art teaching anticipates the claimed invention.

#### *Conclusion*

7. Claim 10 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. Claims 11-13, 15-17, 19-21 and 54 are allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.  
Patent Examiner  
June 4, 2004

*Patrck J. Nolan*  
PATRICK J. NOLAN, PH.D.  
PRIMARY EXAMINER

*6/4/04*